

Amendment and Response

Serial No.: 10/810,738

Confirmation No.: 9703

Filed: 26 March 2004

For: MATERIALS, METHODS, AND KITS FOR REDUCING NON-SPECIFIC BINDING OF MOLECULES TO
A SURFACE

Page 16 of 25

Remarks

The Office Action mailed 9 April 2007 has been received and reviewed. Claims 1-31 are pending. Claims 1, 4, and 15 having been amended, claims 14 and 16-31 having been withdrawn from consideration, and claims 32 and 33 having been added, claims 1-13, 15, 32, and 33 are now pending and under examination. Reconsideration and withdrawal of the rejections are respectfully requested.

Amendments to the Specification

The specification has been amended to correct clear typographical errors in Table 3. Support for the amendments is found, for example, at page 30, lines 10-12, which reads, "Membrane 3 was treated with both the Protein A and the FC4430 but was not eluted. It showed a marked fluorescence indicating that the IgG-FITC was bound." The first sentence supports the amendments to Table 3. The second sentence confirms that any discrepancy between Table 3 and the cited text should be read in favor of the text. The results of Membrane 3 (fluorescence and, therefore, IgG-FITC binding) is consistent with no elution, as stated in the text, and inconsistent with elution, as suggested in Table 3. Moreover, if Table 3 were correct and the cited text incorrect, then Membrane 3 and Membrane 4 would be treated identically, yet provide different results. Applicants respectfully submit that one skilled in the art recognizes the clear error in Table 3. No new matter is introduced by these amendments.

Amendments to the Claims

Claims 1 and 15 have been amended to correct formalities. Support for the amendments exists in claims 1 and 15 as originally filed, and at page 8, lines 11-13.

Claim 4 is amended to correct the claim from which it depends in light of the amendments made herein.

Amendment and Response

Serial No.: 10/810,738

Confirmation No.: 9703

Filed: 26 March 2004

For: MATERIALS, METHODS, AND KITS FOR REDUCING NON-SPECIFIC BINDING OF MOLECULES TO A SURFACE

Page 17 of 25

Claims 32 and 33 recite contacting the solid phase material with a secondary blocking agent. Support for the new claims exists in claims 1 and 15 as originally filed.

No new matter is introduced by the amendments.

Information Disclosure Statements

The Office Action indicates that documents cited by Applicant in an Information Disclosure Statement (IDS) filed September 9, 2004 have not been considered because the IDS allegedly fails to comply with 37 CFR 1.98(a)(2). However, the Office Actions fails to identify how the Information Disclosure Statement fails to comply. Applicants provide herewith a copy of the return postcard indicating receipt by the USPTO of the cited references. Therefore, in the absence of some indication of the manner in which the IDS fails to comply with the requirements of 37 CFR 1.98(a)(2), Applicants reiterate the request that the Examiner initial and return a copy of the Form PTO-1449 to indicate that each document has been considered.

Applicants note that under the rules promulgated by the United States Patent and Trademark Office, the Examiner is obligated to consider and initial documents submitted by Applicants in an IDS:

Examiners must consider all citations submitted in conformance with the rules and this section, and their initials when placed adjacent to the considered citations on the list or in the boxes provided on a form PTO-1449 or PTO/SB/08A and 08B provides a clear record of which citations have been considered by the Office. M.P.E.P. §609(III)(C)(2) (8th Ed.).

Applicants therefore respectfully request that the Examiner initial and return a copy of the Form PTO-1449 to indicate that each document has been considered.

Applicants provide herewith a clean copy of the Form PTO-1449 for the Examiner's convenience.

Amendment and Response

Serial No.: 10/810,738

Confirmation No.: 9703

Filed: 26 March 2004

For: MATERIALS, METHODS, AND KITS FOR REDUCING NON-SPECIFIC BINDING OF MOLECULES TO
A SURFACE

Page 18 of 25

Objections to the Specification

The Office Action sets forth numerous objections to the specification.

MPEP § 608.01 states, “A detailed description of the invention and drawings follows the general statement of invention and brief description of the drawings. This detailed description, required by 37 CFR 1.71, MPEP § 608.01, must be in such particularity as to enable any person skilled in the pertinent art or science to make and use the invention without involving extensive experimentation.” Applicants respectfully submit that Applicants’ disclosure satisfies the requirements of MPEP § 608.01. A response to each objection follows.

At page 8, line 4, the phrase “the non-specific binding of molecules...” is objected to as lacking antecedent basis. Applicants respectfully traverse. There is no requirement that a term in the specification requires antecedent basis before being preceded by a definite article. Moreover, Applicants submit that the phrase “the non-specific binding of molecules...” is clear to a person of ordinary skill in the art, regardless of whether “non-specific binding of molecules” is previously recited in Applicants’ disclosure. Thus, no correction is required. Reconsideration and withdrawal of the objection are respectfully requested.

At page 8, line 5, the phrase “in a target material” is objected to as being unclear because the identity of one or more prepositional reference objects is asserted to be unclear. Applicants respectfully traverse. The phrase “as in” is used as an indicator that the subject matter that follows—a target material—is being used in an exemplary manner. Thus, no correction is required. Reconsideration and withdrawal of the objection are respectfully requested.

At page 8, line 5, the pronoun “which” is objected to as being indefinite. Applicants respectfully disagree. The sentence reads, “It has been surprisingly discovered that the non-specific binding of molecules (e.g., as in a target material) to a solid phase material, which includes a hydrophobic portion, can be decreased by contacting the solid phase material with a fluorinated nonionic surfactant...” Applicants submit that it is clear that “which” begins a non-restrictive parenthetical phrase that refers back to “solid phase material” that immediately

Amendment and Response

Serial No.: 10/810,738

Confirmation No.: 9703

Filed: 26 March 2004

For: MATERIALS, METHODS, AND KITS FOR REDUCING NON-SPECIFIC BINDING OF MOLECULES TO A SURFACE

Page 19 of 25

precedes the parenthetical phrase. Thus, no correction is required. Reconsideration and withdrawal of the objection are respectfully requested.

At page 27, lines 19-20, the phrase "fabricated as described" is objected to as being indefinite. Applicants respectfully disagree. The language objected to is in Example 3 and refers to the fabrication of fibrillated PTFE membranes as described in a preceding Example. The fibrillated PTFE membrane of Example 3 was generally fabricated as described in Example 1 and Example 2, with a certain exception expressly described in Example 3: the membrane of Example 3 is loaded with polypropylene rather than EMPHAZE AB1 (as in Example 1) or EMPHAZE AB1 loaded with Protein A (as in Example 2). Thus, no correction is required. Reconsideration and withdrawal of the objection are respectfully requested.

At page 29, line 1, the phrase "The polypropylene membrane ...used in Example 3." is objected to as lacking antecedent basis. Applicants respectfully disagree. Example 3 describes fabrication of a polypropylene loaded fibrillated PTFE membrane (page 27, lines 18-24), to which the objected to language refers. Thus, no correction is required. Reconsideration and withdrawal of the objection are respectfully requested.

Throughout Example 4, the phrases "CHES buffer" and "CHES/sulfate buffer" are objected to as being unclear. Applicants respectfully disagree. "CHES" is well known to those skilled in the art as referring to a buffer that includes a compound having the formula C₈H₁₇NO₃S, having a formula weight of 207.29, and identified by CAS Registry Number 103-47-9. By various naming conventions, the compound is known as 2-(N-Cyclohexylamino)ethane Sulfonic Acid, N-Cyclohexyl-2-aminoethanesulfonic acid, or 2-(Cyclohexylamino)ethanesulfonic acid, but all refer to the same compound—and same buffer—as demonstrated in the catalog pages submitted by Applicants' herewith. Thus, no correction is required. Reconsideration and withdrawal of the objection are respectfully requested.

At page 29, line 11, the term "They" is objected to as being indefinite. Applicants respectfully disagree. The immediately preceding sentence reads, "Membranes 1 and 2 were not

Amendment and Response

Page 20 of 25

Serial No.: 10/810,738

Confirmation No.: 9703

Filed: 26 March 2004

For: MATERIALS, METHODS, AND KITS FOR REDUCING NON-SPECIFIC BINDING OF MOLECULES TO A SURFACE

treated with the Protein A solution." Applicants submit that it is clear that "They" refers back to the subject of the immediately preceding sentence, Membranes 1 and 2. Thus, no correction is required. Reconsideration and withdrawal of the objection are respectfully requested.

At page 30, line 11, the phrase "was not eluted" is objected to as being indefinite in view of Table 3, column 3. Table 3, column 3 has been corrected, rendering the objection moot.

At page 30, line 13, the pronoun "it" is objected to as being unclear. Applicants respectfully disagree. The preceding sentence reads, "Membrane 4 was treated with both Protein A and FC4430 and was eluted with the elution buffer." Applicants submit that it is clear that "It" refers back to the subject of the immediately preceding sentence, Membrane 4. Thus, no correction is required. Reconsideration and withdrawal of the objection are respectfully requested.

At page 31, line 4, the term "treatment" is objected to as being indefinite. Applicants respectfully disagree. The sentence reads, "Thus, the FC4430 does not cause the removal of a protein adsorbed by hydrophobic interaction before treatment but will prevent adsorption after treatment." Applicants submit that it is clear that "treatment" refers to treating the membrane with FC4430. Thus, no correction is required. Reconsideration and withdrawal of the objection are respectfully requested.

The 35 U.S.C. § 101 Rejection

Claims 1-13 and 15 stand rejected under 35 U.S.C. § 101 as being inoperative and lacking utility. Specifically, the Office Action asserts that Applicants' Examples "appear to accomplish the exact opposite of Applicants' stated intention." (Office Action, page 5). Applicants respectfully traverse.

Claims 1 and 15 are independent claims. Each of claims 2-13 depends, directly or indirectly, from claim 1. Thus, remarks that refer specifically to claim 1 apply equally to claims 2-13 as well. Claim 1 recites a method of reducing non-specific binding of target molecules to a

Amendment and Response

Serial No.: 10/810,738

Confirmation No.: 9703

Filed: 26 March 2004

For: MATERIALS, METHODS, AND KITS FOR REDUCING NON-SPECIFIC BINDING OF MOLECULES TO A SURFACE

Page 21 of 25

surface, while claim 15 recites a method of preparing a solid phase material. Each method includes contacting a solid phase material with a fluorinated nonionic surfactant comprising two or more hydrophobic segments and one or more hydrophilic segments—i.e., a nonionic polymeric fluorosurfactant. The fluorinated nonionic surfactant serves to reduce the extent to which target molecules bind non-specifically to the solid phase material. This effect is demonstrated in Example 3 and Example 4 of Applicants' disclosure.

The Office Action states that the "Examiner did not consider Example 3 because Applicants might have forgotten to add the Protein A." (Office Action, page 5, fn 3). Applicants submit that the omission of Protein A was intended and, indeed, serves to support Applicants' claims and demonstrates the utility of Applicants' invention. By omitting the Protein A, Applicants demonstrate in Example 3 the extent to which the IgG-FITC binds to the membrane in the absence of the Protein A target—i.e., *non-specific* binding. The results (page 28, lines 16-21) indicate that both the untreated membrane and the membrane treated with ZONYL FSG nonionic monomeric fluorosurfactant were highly fluorescent. This fluorescence is an indication of IgG-FITC binding that occurred in the *absence* of the binding target Protein A and is, therefore, non-specific binding. In contrast, the membrane treated with nonionic polymeric fluorosurfactant—a surfactant as recited in Applicants' claims—showed *no* fluorescence, indicating that it had not bound IgG-FITC in the absence of Protein A. Thus, Example 3 demonstrates that treating a membrane with a fluorosurfactant as recited in Applicants' claims reduces non-specific binding of target molecules to the membrane.

Similarly, Example 4 demonstrates that treating a membrane with a fluorosurfactant as recited in Applicants' claims reduces non-specific binding of target molecules to the membrane. Compare Membrane 1 and Membrane 2 in Table 3 at page 30 of Applicants' disclosure. Neither membrane is treated with Protein A, so any binding of IgG-FITC is, by definition, non-specific. Membrane 1 was untreated with fluorosurfactant and, consequently, showed fluorescence, indicating non-specific binding of the IgG-FITC to the membrane (page 30, lines 7-9). In

Amendment and Response

Page 22 of 25

Serial No.: 10/810,738

Confirmation No.: 9703

Filed: 26 March 2004

For: MATERIALS, METHODS, AND KITS FOR REDUCING NON-SPECIFIC BINDING OF MOLECULES TO A SURFACE

contrast, Membrane 2 was treated with a fluorosurfactant as recited in Applicants' claims and showed no fluorescence, indicating that no IgG-FITC was bound. Thus, Membrane 2—the membrane treated with a fluorosurfactant as recited in Applicants' claims—exhibited reduced non-specific binding of target molecules (IgG-FITC) compared to the untreated membrane, Membrane 1.

The Office Action asserts that "Applicants' asserted utilities are premised on experiments that Applicants perform with a certain proprietary composition (*i.e.*, "NOVEC FC4432") that appears to increase binding of molecules to surfaces." (Office Action, page 5, emphasis in original). The Office Action cites Applicants' Example 1 and Example 2 in support of this position. Applicants respectfully submit that the cited Examples support the utility recited in Applicants' claims.

The first columns of Table 1 (Example 1, p. 25) and Table 2 (Example 2, p. 27) each show that a smaller percentage of IgG binds to the membrane treated with the fluorosurfactant than to the membrane treated with TRITON X-100 (Table 1) or unblocked membrane (Table 2). This demonstrated decrease in IgG binding is a decrease in non-specific binding—the very utility recited in the preamble of Applicants' claims. This is shown in the second columns of Table 1 and Table 2, in which a greater percentage of the bound IgG is elutable. The elutable IgG represents IgG that is specifically bound to the Protein A target; non-elutable IgG represents non-specifically bound IgG. Thus, each of Example 1 and Example 2 demonstrates that treating a membrane with a fluorosurfactant decreases non-specific binding of IgG to the membrane.

Applicants respectfully submit that Applicants' Examples demonstrate the utility of the subject matter recited in claims 1 and 15 and respectfully request that the rejection be withdrawn.

The 35 U.S.C. § 112, First Paragraph, Rejection

Claims 1-13 and 15 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey

Amendment and Response

Serial No.: 10/810,738

Confirmation No.: 9703

Filed: 26 March 2004

For: MATERIALS, METHODS, AND KITS FOR REDUCING NON-SPECIFIC BINDING OF MOLECULES TO A SURFACE

Page 23 of 25

to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Specifically, the Office Action asserts that since the claimed invention is not supported by either a credibly asserted utility or a well established utility, one skilled in the art clearly would not want to know how to use the claimed invention.

Applicants respectfully submit that claims 1-13 and 15 do, indeed, recite subject matter that is supported by a credibly asserted utility, as discussed immediately above with respect to the rejection under 35 U.S.C. § 101. Thus, Applicants respectfully submit that claims 1-13 and 15 meet the requirements of 35 U.S.C. § 112, first paragraph, and request that the rejection be withdrawn.

The 35 U.S.C. § 112, Second Paragraph, Rejection

Claims 1-13 and 15 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Specifically, claims 1 and 15 are asserted to be incomplete for omitting essential steps. Claims 1 and 15 are further asserted to be incomplete for omitting essential structural cooperative relationships between elements.

The term "contacting" in claim 1 is asserted to be indefinite because "the identity of two or more objects subject to 'contacting' is not clear (Office Action, page 7). Applicants disagree.

In each occurrence of the term "contacting," the objects to be contacted are clearly recited. In each occurrence, Applicants use the following form: contacting A with B...

For example (emphasis added):

contacting the solid phase material with the fluorinated nonionic surfactant...

contacting the solid phase material with the sample...

Applicants submit that use of the term "contacting" in the claims is clear and therefore meets the requirements of 35 U.S.C. § 112, second paragraph.

Amendment and Response

Serial No.: 10/810,738

Confirmation No.: 9705

Filed: 26 March 2004

For: MATERIALS, METHODS, AND KITS FOR REDUCING NON-SPECIFIC BINDING OF MOLECULES TO A SURFACE

Page 24 of 25

The Office Action asserts that the phrase "the solid phase material with the fluorinated nonionic surfactant" lacks antecedent basis. Applicants respectfully disagree. Both materials—i.e., the solid phase material and the fluorinated nonionic surfactant—are expressly recited in a "providing" step earlier in the claim.

The Office Action asserts that the phrase "the solid phase material with the secondary blocking agent" lacks antecedent basis. Applicants respectfully disagree. Both materials—i.e., the solid phase material and the secondary blocking agent—are expressly recited in a "providing" step earlier in the claim.

The Office Action asserts that the phrase "the blocked solid phase material with the sample" lacks antecedent basis. Applicants respectfully disagree. Both materials—i.e., the blocked solid phase material and the sample—are expressly recited in a "providing" step earlier in the claim.

The Office Action asserts that the phrases "contacting the blocked solid phase material" and "contacting the blocked solid phase material with the sample" are indefinite when a secondary blocking agent is not provided. Applicants respectfully disagree. The fluorinated nonionic surfactant blocks non-specific binding and is, therefore, a blocking agent. It is, indeed, implicitly serving as a "primary" blocking agent. Thus, contacting the solid phase material with the fluorinated nonionic surfactant to block at least a portion of the hydrophobic portion of the solid phase material provides antecedent basis for "contacting the blocked solid phase material" even when no secondary blocking agent is provided and contacted with the solid phase material.

The Office Action asserts that the infinitive "to adhere" is indefinite. While not necessarily agreeing with the position stated in the Office Action, Claim 1 has been amended to recite that the blocked solid phase material is contacted with the sample "so that at least a portion of the target molecules of the sample adheres to the capture sites."

Applicants submit that claims 1-13 and 15 satisfy the requirements of 35 U.S.C. §112, second paragraph and respectfully request that the rejection be withdrawn.

Amendment and Response

Serial No.: 10/810,738

Confirmation No.: 9703

Filed: 26 March 2004

For: MATERIALS, METHODS, AND KITS FOR REDUCING NON-SPECIFIC BINDING OF MOLECULES TO A SURFACE

Page 25 of 25

Summary

It is respectfully submitted that the pending claims 1-13, 15, 32, and 33 are in condition for allowance and notification to that effect is respectfully requested. The Examiner is invited to contact Applicants' Representatives, at the below-listed telephone number, if it is believed that prosecution of this application may be assisted thereby.

Respectfully submitted
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July 5, 2007
Date

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CERTIFICATE UNDER 37 CFR §1.8:

The undersigned hereby certifies that the Transmittal Letter and the paper(s), as described hereinabove, are being transmitted by facsimile in accordance with 37 CFR §1.6(d) to the Patent and Trademark Office, addressed to Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 5th day of July, 2007, at 10:32 am (Central Time).

By: Dani Moroz
Name: Dani MOROZ